I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4).

Dated: May 21, 2008
Electronic Signature for Colleen McKiernan, Ph.D.: /Colleen McKiernan, Ph.D./

Docket No.: 68138(46590)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Takahito Hara et al.

Application No.: 10/516,705

Confirmation No.: 1003

Filed: December 2, 2004

Art Unit: 1643

For: MUTANT ANDROGEN RECEPTOR, CANCER CELLS EXPRESSING THE SAME, A METHOD OF PRODUCING THEM AND USE THEREOF

Examiner: L. A. Bristol

REMARKS: PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The following remarks support Applicant's "Pre-Appeal Brief Request for Review" filed herewith in the above-referenced application. These remarks constitute no more than five pages, and are being filed with a Notice of Appeal, thereby satisfying the requirements.

Claims 73 and 75 are rejected under 35 U.S.C. §112, ¶2 as being indefinite for failing to particularly point out and distinctly claim the subject matter. The Advisory Action states that if the amendments were entered, the rejection would be overcome. This rejection is not further addressed herein.

Claims 12, 71, 72, and 74-76 are rejected under 35 U.S.C. §112, ¶1 for allegedly failing to comply with the written description requirement for allegedly containing new matter which was not described in the specification. This rejection is respectfully traversed.

Claim 73 is rejected under 35 U.S.C. §112, ¶1, because the specification allegedly does not enable one skilled in the art to use the invention as the specification does not provide evidence that the biological materials are known and readily available to the public, or reproducible from the written description. In the Advisory Action, claims 74-76 were added to

the rejection. This rejection is respectfully traversed.

Applicant respectfully requests review of the Final Office Action in the above referenced application. No amendments are being filed with this request.

Applicant is filing the "Pre-Appeal Brief Request for Review" based on the following clear errors and/or omissions in the Final Office Action mailed on January 4, 2008 and the Advisory Action mailed on April 22, 2008.

First Clear Error and/or Omission in the Final Office Action

The Examiner has made a first clear error and/or omission for rejecting claims 12, 71, 72, and 74-76 for failing to comply with the written description requirement for containing new matter. The Office Action states that the "disclosure cannot in any way be interpreted as providing literal or implicit support for the instant claimed recitation" of "for at least three months " (Final Office Action, page 7). Yet, later in the same paragraph the Office Action states that the "only other support for any other duration of a culture period appears in Example 1 of the specification ... where proliferating clones were identified after 6 and 13 weeks." This clearly supplies at least implicit support for "at least three months" as the test for support is not an *in haec verba* requirement (see Response to Final Office Action mailed on March 25, 2008).

Moreover, the Office Action states that the instant claims recite no upper limit for the amount of time in culture in the new matter rejection. A new matter rejection cannot be made over an element not included in the claims.

The Office Action further states that "Applicants are required to identify by showing... where a cancer cell should be "cultured for at least three months" in the presence of an antiandrogen test substance in order to identify a drug that a) suppresses proliferation of the cancer cell and b) does not induce antiandrogen drug resistance" (as stated on page 7 of the Final Office Action).

Claims 12 and 71-76 are drawn to methods of screening, not a test substance having particular properties. The methods include culturing a cell in the presence of a test substance, to identify a test substance that suppresses proliferation of the cancer cells, but does not induce antiandrogen drug resistance. Applicant has provided culture conditions, cells, and test substances for use in the method of the invention.

The methods of claims 12, 71 and 72 use a androgen-sensitive cancer cell in the screening method.

The methods of claims 73 to 76 use an androgen-insensitive cancer cell in the screening method having a mutation at amino acid 746 of SEQ ID NO: 2 (the androgen receptor, e.g., see page 73, line 33 to page 74, line 8).

Example 1 in the specification teaches that proliferation of androgen sensitive cells can be suppressed for three months without killing all of the cells in the culture (see page 78 of the specification, page 13 and 14 of the response to Final Office Action mailed March 25, 2008). Upon exposure of prostate cancer cells to a compound known to induce antiandrogen drug resistance, cells "did not proliferate initially. However, ... two cell lines exhibiting proliferation were obtained."

The methods of claims 12, 71, and 72 are essentially the same as the method of Example 1, except for selection of the test compounds. The methods of claims 73 to 75 are essentially the same as the methods of claims 12, 71, and 72, except for selection of the cell type. In both groups of claims, cells are cultured for at least three months, wherein proliferating cells are indicative of compounds that promote anti-androgen drug resistance.

Cells that can be used in the screening methods of claims are taught in the specification, for example, on page 17, line 31-page 18, line 3 and page 30, lines 18-21.

Culture conditions are provided, for example, on page 32, lines 16-23.

Test compounds that can be used in the screening methods of the invention are provided, for example, on page 51, line 29 to page 60, line 17. A compound identified to inhibit activity of a W741C androgen receptor in Example 5 (page 79, lines 19-25).

Therefore, each of the elements required to practice the claimed methods is provided by the specification.

The Examiner states that the claims recite a lower limit, but no upper limit in regard to the time in culture. At least two biologically defined endpoints are inherent in the methods. First, the cell develops resistance to the test compound. Second, all of the cells in the culture die. Additional time in culture will not provide further information. Upon identification of resistant cells in less than three months, the compound fails to meet the desired characteristics of

the screen. This endpoint is clearly contemplated in the methods. Applicant further submits that it is well known that cells in culture will eventually die if they do not proliferate, providing an endpoint to the screening method. Moreover, selection of arbitrary endpoints for experiments is well known in the art. No explicit endpoint is required.

Second Clear Error and/or Omission in the Final Office Action

The Examiner has made a second clear error and/or omission for rejecting claim 73 in the Final Office Action, and further rejecting claims 74-76 in the Advisory Action for lack of enablement in requiring a biological deposit. The Examiner states that a biological deposit is required as "the specification does not provide evidence that the claimed biological materials are (a) known and readily available to the public; and (b) reproducible from the written description." Applicant respectfully disagrees.

Applicant submits that methods of generation of cell lines expressing a protein of the claimed is routine in the art. The mutant AR nucleic acid for expression of the claimed protein of the invention can be derived from essentially any cell type (see page 12, line 35-page 13, line 17; page 17, line 31-page 18, line 3). Cloning of the DNA can be performed by PCR or other methods (page 27, lines 25-35) and inserted into any of a number of available plasmids or expression constructs (page 28, lines 19-23) including an appropriate promoter (page 28, line 25-page 29, line 2), and optionally containing other transcriptional regulatory sequences (page 29, lines 4-12). The expression vector can be transformed into a cell using any of a number of known methods (page 31, lines 1-4) or any of a number of commercially available kits (see Examples 4 and 6) known to those of skill in the art. The specification further includes methods for obtaining cell lines from transgenic mice expressing the desired form of AR (page 64, line 26ff).

Working examples of generation of expression vectors (reference Example 1), methods of transfection are taught (Examples 4 and 6) in the specification.

"The description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption" (MPEP 2163.04 and *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). Furthermore, the Examiner "must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of the

evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims (*In re Wertheim*, 541 F.2d at 263, 191 USPQ at 97 (CCPA 1976)). 35 U.S.C. 112 requires the specification to be enabling only to a person "skilled in the art to which it pertains, or with which it is most nearly connected." The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. (*In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.,* 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)). Applicant submits that methods of expression construct generation and cell transfection are well known in the art. Moreover, method to detect cells expressing the desired AR are well known in the art.

No deposit is required where the required biological materials can be obtained from publicly available material with only *routine experimentation and a reliable screening test.* (*Tabuchi v. Nubel*, 559 F.2d 1183, 194 USPQ 521 (CCPA 1977); *Ex Parte Hata*, 6 USPQ2d 1652 (Bd. Pat. App. & Int. 1987). Applicant requests that the Examiner provide support for the allegation that methods of expression vector selection and generation, and methods of cell transformation are not well within the ability of those of skill in the art. No biological deposit is required.

Applicant submits that all of the claims under final rejection are in condition for allowance and should be allowed, and that the Final Office Action should be withdrawn.

Dated: May 21, 2008

Respectfully submitted,
Electronic signature: /Colleen McKiernan, Ph.D./
Colleen McKiernan, Ph.D.
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5555
Registration No.: 48,570
Attorneys/Agents For Applicant